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CASE REPORT

BEGINNER

CLINICAL CASE

Pulmonary Artery Pressure Ventricularization in a Patient With Carcinoid Heart Disease

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ABSTRACT

Ventricularization of the pulmonary artery pressure curve is shown, characterized by a steep diastolic pressure fall with mid-diastolic pressure equalization with the right ventricle, which was caused by severe pulmonary valvular regurgitation in a patient with carcinoid heart syndrome. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:1200–4)
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A 72-year-old man was referred for further diagnostic workup because of progressive dyspnea, recurrent symptomatic ascites, and renal failure on September 6, 2019. At admission, the patient was in reduced general condition and had pronounced dyspnea (New York Heart Association functional class IV) and orthopnea. Vital signs on presentation: temperature: 35.8°C; pulse: 63 beats/min; blood pressure 111/56 mm Hg; respiratory rate: not documented. Blood analysis revealed increased levels of N-terminal pro-B-type natriuretic peptide (8.523 pg/ml), renal retention parameters (creatinine: 291 μmol/l) and pathologic hepatic enzymes (γ-glutamyltransferase: 183 U/l; alkaline phosphatase: 328 U/l).

LEARNING OBJECTIVES

- To understand the high adaptive capacity of the right ventricle in tolerating massive volume overload caused by free pulmonary valve regurgitation.
- To consider carcinoid heart syndrome as the cause of massive pulmonary valve regurgitation aside from pulmonary valve stenosis.

PAST MEDICAL HISTORY

The patient was first diagnosed in 2007 with a neuroendocrine tumor of the small intestine (pT3 pN1, L1 V0 G1) with hepatic metastases; diagnosis was followed by immediate resection of the primary tumor. Subsequently, he underwent several cycles of medical therapy with octreotide, everolimus, and lanreotide, resulting in a stable, progression-free state according to the oncologist in charge. In June 2017, severe tricuspid valve regurgitation as the first manifestation of carcinoid heart syndrome led to tricuspid valve replacement surgery using a biological valve prosthesis. Transthoracic echocardiography of the other cardiac valves showed only mild structural alterations at that time.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

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DIFFERENTIAL DIAGNOSIS

In July 2019, transthoracic echocardiography revealed a good surgical result without residual tricuspid regurgitation. Furthermore, a dilated right ventricle (RV) with severely impaired systolic function and left ventricular (LV) infero-posterolateral thickening of the pericardium was visualized. Together with the known episodes of ascites, post-operative constrictive pericarditis was suspected with right heart failure in the context of the preceding tricuspid regurgitant RV volume overload.

INVESTIGATIONS

Accordingly, left and right heart catheterization was performed for evaluation of the hemodynamic situation. Even after fluid challenge (approximately 1 l), the diagnosis of constrictive pericarditis could not be confirmed hemodynamically. Pulmonary artery (PA) pressure (PAP) was significantly increased (mean PAP: 34 mm Hg), and the phasic PAP curve was entirely congruent with the phasic RV pressure curve upon catheter pullback (**Figure 1A**). Thus, there was a complete loss of function of the pulmonary valve with free regurgitation.

In this context, the steep diastolic blood pressure decrease was caused by the unconstrained regurgitation followed by PA-RV pressure equilibrium and a subsequent mid-diastolic pressure increase once RV compliance was exhausted. These particular hemodynamics were alternatively imaged by continuous-wave Doppler echocardiography (**Figure 1B**, Video 1), which shows early diastolic termination of the regurgitant flow velocity signal. Late diastolic atrial contraction was imaged by continuous-wave Doppler as the flow velocity signal having the same direction as RV ejection (i.e., a-wave). Accordingly, the evidence of the a-wave in the PA verified the loss of function of the pulmonary valve.

The hemodynamic situation was modeled by using a hemodynamic simulator (1). The combination of free pulmonary valve regurgitation with impaired RV diastolic relaxation, in the absence of tricuspid valve regurgitation and preserved right atrial function, produced identical RV and PA phasic pressure curves as well as the biphasic diastolic flow signal in the PA (**Figures 2B and 2C**). In addition, RV volume overload caused impaired LV filling due to ventricular interdependence resulting in systemic sequelae, such as chronic pre-renal kidney failure.

MANAGEMENT

Because of the patient's refusal of another surgical intervention, transcatheter pulmonary valve implantation was successfully performed by a

ABBREVIATIONS AND ACRONYMS

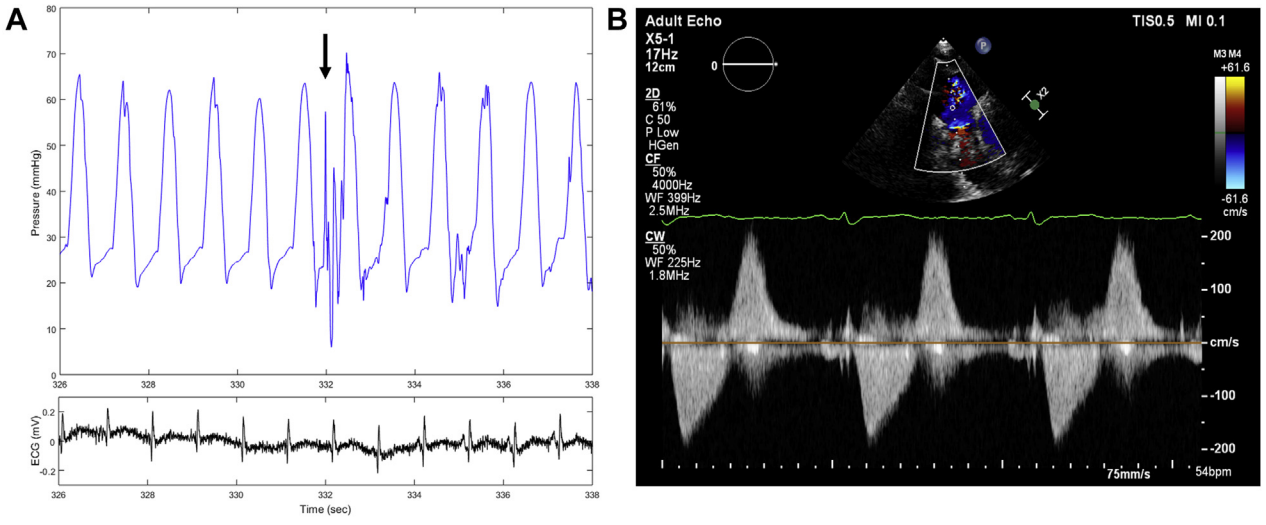
LV = left ventricle

PA = pulmonary artery

PAP = pulmonary artery pressure

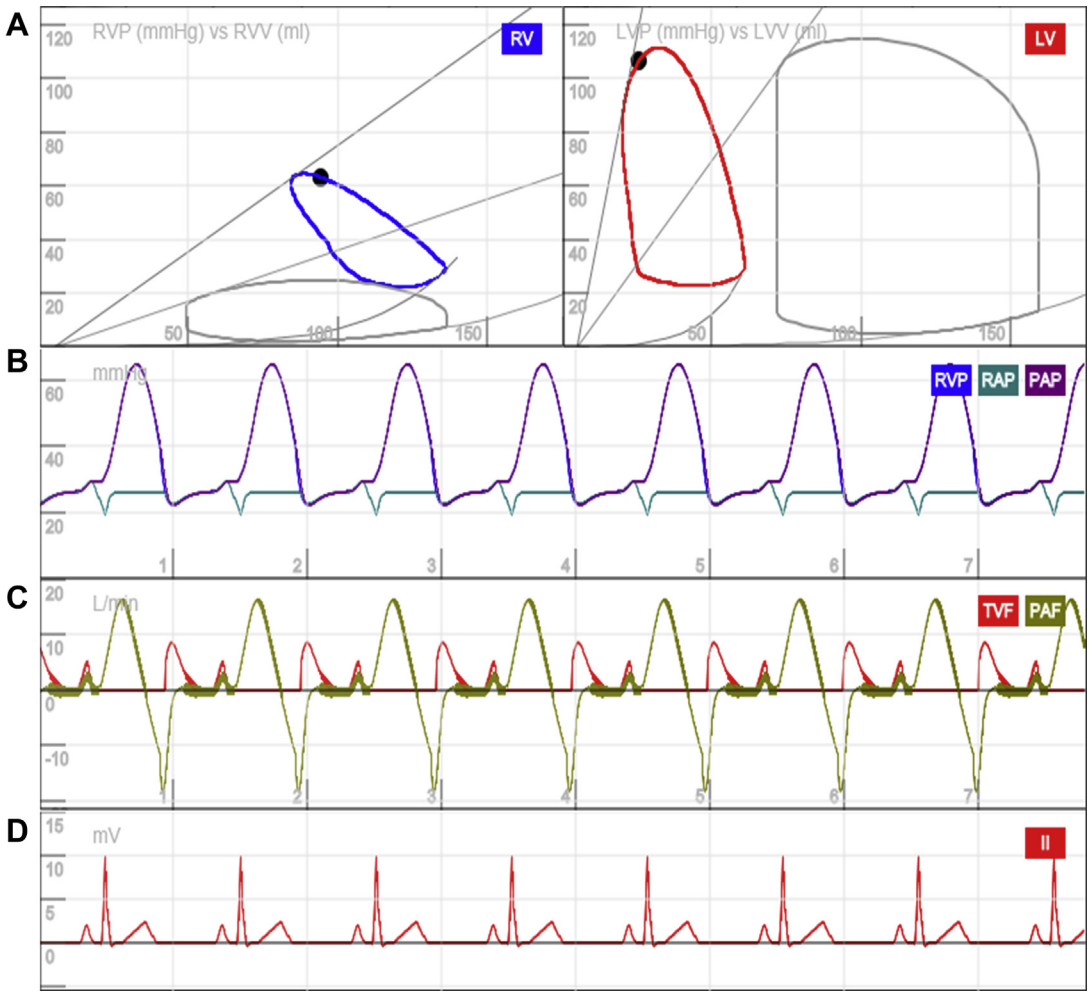
RV = right ventricle

FIGURE 1 Pulmonary Artery Pressure Ventricularization



(A) Recording of the pressure curve in the pulmonary artery with pullback of the catheter into the right ventricle (marked by an **arrow**). Please note the ventricular morphology of the pulmonary artery pressure curve because of the complete loss of function of the pulmonary valve. **(B)** The pressure measurement was confirmed by transthoracic echocardiography, showing a triphasic continuous-wave Doppler signal in the pulmonary artery referring to the ejection, the regurgitation, and the atrial contraction phase.

FIGURE 2 Hemodynamic Simulation Using an Online Software (1)



(A) Pressure-volume loops of the right and left ventricles (RV and LV), including lines for the end-systolic pressure-volume relationship (end-systolic elastance) and end-diastolic pressure-volume relationship (ventricular compliance). The **loops in gray** represent the hemodynamic situation of a healthy person. **(B)** Pressure curves of the right ventricle (RVP), the right atrium (RAP), and the pulmonary artery (PAP). Please note the early diastolic pressure equalization. **(C)** Flow pattern through the tricuspid valve (TVF) and in the pulmonary artery (PAF). As an expression of the mid-diastolic pressure equalization between the RV and pulmonary artery, PAF in the same period oscillates around 0. **(D)** Electrocardiogram, lead II.

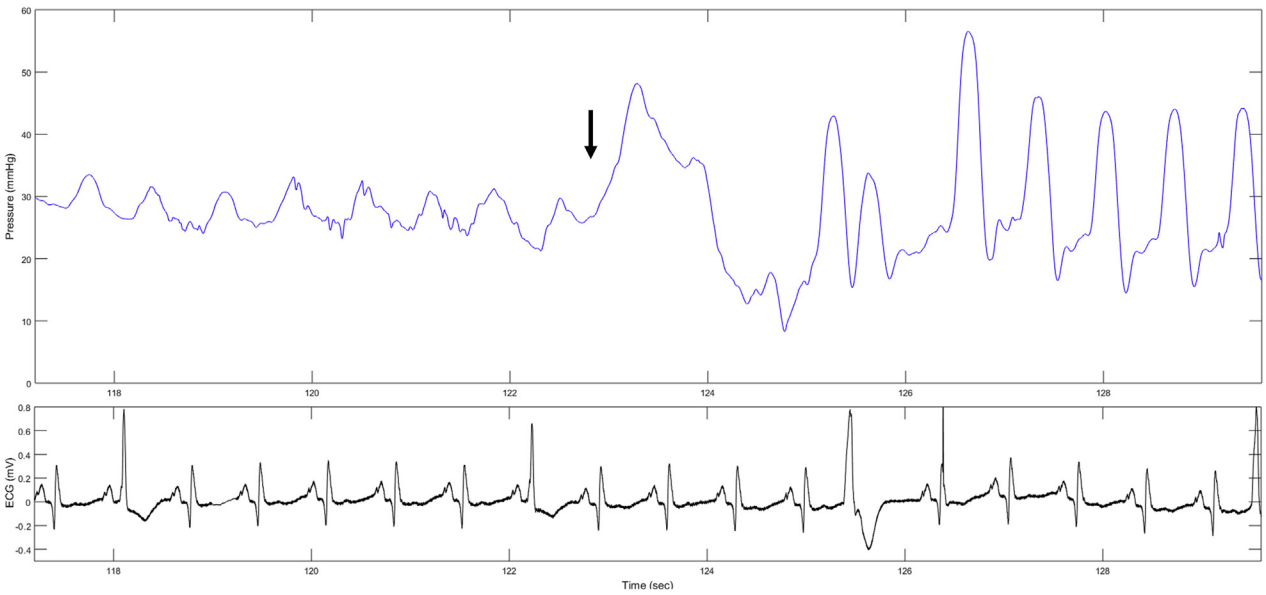
balloon-expandable biological valve (Edwards Sapien 3, 29 mm, Edwards Lifesciences, Irvine, California).

After pulmonary valve prosthesis implantation, recording of the PAP revealed immediate normalization and a decrease in mean PAP (Figure 3). Catheter pullback into the RV showed an unchanged RV pressure curve and mild pulmonary stenosis, with a peak-to-peak gradient of 11 mm Hg, as an expression of still augmented-RV stroke volume (i.e., a functional stenosis).

DISCUSSION

The presented case shows rapidly progressive carcinoid heart disease despite extended oncological therapy, tricuspid valve replacement for severe insufficiency, and symptomatic treatment for recurrent right heart failure. The reason for this course of events is disease progression involving the pulmonary valve, culminating in its functional absence with PAP (right) ventricularization. In carcinoid syndrome, high plasma levels of vasoactive

FIGURE 3 **Normalization of the PAP Curve Immediately After Prosthesis Implantation**



Recording of the pressure curve in the pulmonary artery after implantation of the bioprosthesis with pullback of the catheter into the right ventricle; the beginning of the pullback is marked by an **arrow**. Please note the immediately normalized pulmonary artery pressure curve morphology, including the notching at the beginning of the diastole as well as a continuously diastolic decrease of the pressure. ECG = electrocardiogram.

substances such as serotonin, prostaglandins, and histamine cause mitogenic effects on fibroblasts and smooth muscle cells, resulting in plaque-like depositions on the endocardial surfaces of valves and the subvalvular apparatus (2). The spectrum of these pathological modifications stretches from functionally negligible, mild valvular thickening to complete fixation of valvular leaflets and cusps. Because of pulmonary inactivation of the vasoactive substances, right heart valves are predominantly affected, except for patients with right-left shunts (e.g., persistent foramen ovale) (2).

Concerning the optimal treatment of patients with carcinoid heart disease, an expert statement is available from the International Symposium for Carcinoid Heart Disease held in 2014 in London, United Kingdom (2) (summary listed in **Table 1**).

The high adaptive capacity of the RV to the massive volume overload caused by free pulmonary valve regurgitation is remarkable. Today, such clinical cases are rare because of improved diagnostic methods, and they are mostly restricted to the right side of the heart. Historically, rare cases of very severe aortic valve regurgitation with late-diastolic aortic valve opening in response to left atrial contraction following arterial and LV pressure equalization have been described (3).

However, our case is special with regard to the underlying carcinoid heart syndrome, which functionally dissolved the pulmonary valve. Thus, severe pulmonary valve regurgitation caused diastolic elastic recoil of the overdistended RV myocardium as a probable mechanism for the mid-diastolic pressure increase, which followed PA-RV pressure equilibration. Preserved right atrial function induced the end-

TABLE 1 **Summary of the Expert Statement (2)**

Biomarkers for heart involvement in carcinoid syndrome
• N-terminal pro-B-type natriuretic peptide, cutoff level: 260 pg/ml • Plasma/urinary 5-hydroxyindoleacetic acid (metabolization product of serotonin)
Diagnostic imaging modalities
• Transthoracic echocardiography (gold standard) Optionally including advanced echocardiographic techniques (3-dimensional) • Cardiac computed tomography Assessment of the degree of structural valvular damage, pre-surgical assessment • Cardiac magnetic resonance imaging Quantification of ventricular volumes, impaired echocardiographic quality
Treatment
• Pharmacotherapy for heart failure • Control of carcinoid syndrome symptoms Gold standard: long-acting formulations of somatostatin analogues (octreotide and lanreotide) • Surgical management of carcinoid heart disease Primarily valve replacement with adequate pre-surgical assessment, including renal, liver, and lung function tests • Percutaneous catheter-based interventions in high-risk patients with severe carcinoid heart disease

diastolic antegrade pressure /flow velocity wave, the detection of which in the pulmonary trunk proves, on its own, complete absence of pulmonary valvular function.

FOLLOW-UP

The day after prosthesis implantation, transthoracic echocardiography revealed correct positioning with mild paravalvular regurgitation along with the known pressure gradient across the prosthesis (Video 2). Respiratory variability of the inferior vena cave suggested normal central venous pressure (5 to 10 mm Hg). Three days later, the patient described a significant improvement of his condition and was referred for cardiac rehabilitation. During rehabilitation, the patient expressed being exhausted from medical treatment and his wish to die. After extensive discussion with his spouse and relatives, oral medication was stopped, and palliative care was introduced. The patient died 2 months later.

CONCLUSIONS

Functional absence of the pulmonary valve caused by carcinoid heart disease resulted in free pulmonary regurgitation, causing phasic PAP to merge with RV pressure, that is, to completely ventricularize. This situation, although compatible with life, causes multiple organ dysfunction based on impaired LV filling with insufficient stroke volume.

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KEY WORDS cancer, insufficiency, pulmonic valve, right ventricle

APPENDIX For supplemental videos, please see the online version of this paper.